

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Data Requirement:	PMRA Data Code	{.....}
	EPA DP Barcode	353315
	OECD Data Point	{.....}
	EPA MRID	473723-45
	EPA Guideline	OPPTS 850.2300

Test material:	AE C656948	Purity: 94.7%
Common name	Fluopyram	
Chemical name:		
	IUPAC: N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}- α,α,α -trifluoro-o-toluamide	
	CAS: N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide	
	CAS No.: 658066-35-4	
	Synonyms: None reported	

Reference/Submission No.: {.....}

Company Code	{.....}	[For PMRA]
Active Code	{.....}	[For PMRA]
Use Site Category	{.....}	[For PMRA]
EPA PC Code	080302	

CITATION: Stoughton, T.L., and C.V. Lam. 2008. Effect of AE C656948 Technical on Reproduction of the Northern Bobwhite Quail. Unpublished study performed by Bayer CropScience, Stilwell, KS. Laboratory Project No. EBGMP004. Study sponsored by Bayer CropScience, Research Triangle Park, NC. Study initiated October 18, 2006 and submitted April 7, 2008 (amended report).

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EXECUTIVE SUMMARY

The one-generation reproductive toxicity of AE C656948 (fluopyram) to 18 pairs per level of 16-week old Northern bobwhite quail (*Colinus virginianus*) was assessed over *ca.* 23 weeks. AE C656948 was administered to the birds in the diet at nominal concentrations of 0 (control), 250, 500, or 1000 mg ai/kg diet (adjusted for purity). Mean-measured concentrations were <9.61 (<LOQ, control), 237, 530, and 1082 mg ai/kg diet, respectively. Due to significant effects upon reproduction at all treatment levels, the recovery potential was examined at the 530 and 1082 mg ai/kg diet levels during the final 4 weeks of egg production.

The reviewer's analysis revealed a significant adverse effect on adult female body weight gain at the lowest treatment level during the first five-week egg laying period, as well as significant ($p \leq 0.05$) treatment-related effects upon most reproductive endpoints at all treatment levels. Effects included reductions in the numbers of eggs laid, increases in the numbers of cracked or defective eggs, increases in embryonic mortality, reductions in egg shell strength and thickness, and reductions in the numbers of hatchlings and 14-day old survivors. In addition, the body weights of offspring and 14-day old survivors were inhibited 14-26% at the 530 and 1082 mg ai/kg diet levels compared to the controls.

Positive results were observed for most reproductive endpoints during the 4-week recovery period (relative to untreated birds at these levels). For both the 530 and 1082 mg ai/kg diet levels, increases were observed in the numbers of eggs laid, eggs set, viable embryos, live 18-day embryos, hatchlings, and 14-day old survivors, and a decrease was observed in the number of cracked eggs. However, a decrease in the number of defective eggs and increases in hatchling and 14-day old survivor body weights were only clearly observed at the 530 mg/kg diet level during the recovery period. Egg shell strength and thickness improved notably at both levels, where values obtained during recovery approached control levels.

This study is **scientifically sound/unsound** and **{does or does not}** satisfy the guideline requirement for a Northern bobwhite quail (*Colinus virginianus*) reproductive toxicity study.

Results Synopsis

Test Organism Size/Age (mean Weight): 16-weeks old; 171-217 g (combined sexes)

NOAEC: <237 mg ai/kg diet

LOAEC: 237 mg ai/kg diet

Endpoint(s) Affected: adult female weight gain and all reproductive and offspring endpoints

Most Sensitive Endpoint(s): adult female weight gain and all reproductive and offspring endpoints

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I. REPORTED MATERIALS AND METHODS

GUIDELINE FOLLOWED: U.S. EPA Pesticide Assessment Guidelines, Series 71-4 (1982)
OECD Guideline for Testing of Chemicals, No. 206 (1984)
U.S. EPA Ecological Effects Test Guidelines, OPPTS 850.2300 (1996)

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. This study was conducted in compliance with the U.S. EPA 40 CFR Parts 160 with the following exceptions: basal diet screening analysis, and support files were not located for analytical balance verification (10/12/06 and 10/30/06).

A. REPORTED MATERIALS:

1. Test Material

Table 1: Test material.

Parameter	Details
Name	AE C656948 (fluopyram)
Description	Solid
Lot No./Batch No.	08528/0002
Purity	94.7%
Stability under test conditions	Verified in treated feed under frozen storage for 12 weeks and ambient storage for 10 days.
Storage conditions	Ambient

Table 2: Physicochemical properties of fluopyram.

Parameter	Values
Water solubility at 20°C	Not reported
Vapor pressure	Not reported
UV absorption	Not reported
pKa	Not reported
Kow	Not reported

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2. Test organism:

Table 3: Test organism.

Parameter	Details
Species (common and scientific names):	Northern bobwhite quail (<i>Colinus virginianus</i>)
Age at Study Initiation:	16 weeks old
Body Weight: (mean and range)	Males: Overall range (n=72) of 171 to 217 g, with group means of 192 to 196 g. Females: Overall range (n=72) of 175 to 204 g, with group means of 189 g.
Source:	WW Quail Ranch, Wardville, OK

B. REPORTED STUDY DESIGN:

1. Experimental Conditions

a. Range-finding study: None.

b. Definitive Study:

Table 4: Experimental Parameters.

Parameter	Details
Acclimation period:	2 weeks
Conditions (same as test or not):	Same as test
Feeding:	Teklad Starter Ration during acclimation and Teklad Game Bird Ration during testing, <i>ad libitum</i> Tap water, <i>ad libitum</i> .
Health (any mortality observed):	Not reported

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Parameter	Details
<u>Test duration</u> pre-laying exposure: egg-laying exposure: withdrawal period, if used:	14 weeks 9 weeks Final 4 weeks of the egg-laying period, half of the 250 and 500 mg/kg replicates only
<u>Pen (for parental and offspring)</u> size: construction materials: number:	Parental: 56 (L) x 28 (W) x 27 (H) cm Offspring: 91 (L) x 81 (W) x 25 (H) cm Parental: stainless steel wire grid and sheeting Offspring: galvanized wire mesh and sheeting 18 parental pens/treatment level. Hatchlings were group-housed according to the appropriate parental concentration.
Number of birds per pen (male:female)	2 birds/pen (1 male:1 female)
<u>Number of pens per group/treatment</u> negative control: solvent control: treated:	18 pens N/A 18 pens/treatment
<u>Test concentrations (mg ai/kg diet)</u> nominal: measured:	0 (negative control), 250, 500, and 1000 mg ai/kg diet <9.61 (<LOQ, control), 237, 530, and 1082 mg ai/kg diet, respectively
Maximum labeled field residue anticipated and source of information:	Not specified
Solvent/vehicle, if used type: amount:	N/A
Was detailed description and nutrient analysis of the basal diet provided? (Yes/No)	Yes

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Parameter	Details
Preparation of test diet	The study authors reported that approximately every 10 days, the appropriate amount of sieved AE C656948 was blended with a portion of basal diet in a Kitchen Aid mixer for ≥ 5 minutes. The blended mix was added to <i>ca.</i> half of the basal ration and mixed using a Hobart mixer for ≥ 5 minutes. The remaining half of the basal diet was added, and the treated feed mixed for at least an additional 5 minutes. If not used immediately after mixing, diets were reportedly stored in covered plastic containers at -12°C.
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes
Were concentrations in diet verified by chemical analysis?	Yes
Did chemical analysis confirm that diet was stable? and homogeneous?	Yes Yes
Feeding and husbandry	Feeding and husbandry conditions appeared to be adequate, given guideline recommendations.
<u>Test conditions</u> temperature: relative humidity: photoperiod: light intensity: air exchanges:	Mean of 21.3 °C Mean of 54.7% 7 hr light/day up through Week 8; 17 hr light/day thereafter 5.9 to 17.8 ft. candles 12 volumes per hour
Egg Collection and Incubation	
<u>Egg collection and storage</u> collection interval: storage temperature: storage humidity:	Twice daily Mean of 12.0°C Mean of 87.7%
Were eggs candled for cracks prior to setting for incubation?	Yes
Were eggs set weekly?	Yes
When candling was done for fertility?	Day 11 (embryo viability) Day 18 (embryo survival)

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Parameter	Details
When the eggs were transferred to the hatcher?	Day 21
<u>Hatching conditions</u> temperature: humidity: photoperiod:	Not reported Not reported 14 hours light/10 hours dark (hatchlings)
Day the hatched eggs were removed and counted	Days 24 or 25
Were egg shells washed and dried for at least 48 hrs before measuring?	Yes
<u>Egg shell thickness</u> no. of eggs used: intervals: mode of measurement:	All eggs laid One day every other week throughout the egg laying period Three points around the equatorial circumference to the nearest 0.001 mm
Reference chemical, if used	None used

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2. Observations:

Table 5: Observations.

Parameter	Details
Parameters measured	
<u>Parental</u>	<ul style="list-style-type: none"> - mortality - body weight - food consumption - signs of toxicity - necropsy
<u>Egg collection and subsequent development</u>	<ul style="list-style-type: none"> - eggs laid - eggs cracked - egg defective - egg shell thickness - egg shell strength - eggs set - viable embryos - live 18-day embryos - number of hatchlings - hatchling body weight - number of 14-day-old survivors - 14-day-old survivor body weight - signs of toxicity of hatchlings - recovery potential
Indicate if the test material was regurgitated	No indications of dietary regurgitation.
Observation intervals (for various parameters)	Parental mortality and signs of toxicity: daily Parental body weights: Weeks 1, 3, 5, 7, 9, and 23 Parental food consumption: weekly through Week 19 Offspring mortality and signs of toxicity: daily Offspring body weights: 0 and 14 days
Were raw data included?	Yes

II. REPORTED RESULTS:

A. REPORTED MORTALITY:

Six incidental adult mortalities (all female) occurred during the study: one in the control group, two in the 250 mg ai/kg diet group, one in the 500 mg ai/kg diet group, and two in the 1000 mg ai/kg diet group. The study authors reported that the mortalities were considered random and not related to treatment.

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Table 6: Effect of AE C656948 (Fluopyram) on Mortality of Northern Bobwhite.

Treatment (mg ai/kg diet) Mean-measured (and Nominal) Concentrations	Observation Period ^(a)					
	Week 8		Week 15		Week 23	
	No. Dead		No. Dead		No. Dead	
	Male	Female	Male	Female	Male	Female
Control	0	0	0	0	0	1
237 (250)	0	0	0	1	0	2
530 (500)	0	0	0	1	0	1
1082 (1000)	0	0	0	1	0	2

^(a) Includes a 4-week recovery period for half of the replicates from the 500 and 1000 mg ai/kg diet levels.

B. REPORTED REPRODUCTIVE AND OTHER ENDPOINTS:

Abnormal Effects/Behavior: No treatment-related clinical signs of toxicity were observed at any treatment level. The study authors reported that minor occurrences of feather loss were observed at all levels beginning during Week 12 and continuing throughout the remainder of the study. In addition, it was reported that several birds in the 250 and 500 mg ai/kg diet groups exhibited injuries and/or lacerations as a result of normal cage wear and/or pen-mate aggression.

Food Consumption: The study authors reported that since a recovery period was incorporated into the final 4 weeks of the study, food consumption was calculated only to Week 19. No statistically-significant differences were observed at any treatment level for feed consumption, which averaged 18.5, 19.5, 19.7, and 20.5 g/bird/day for the control, 250, 500, and 1000 mg ai/kg diet levels, respectively. It was reported that although no statistics were performed for the treated versus untreated replicates during the recovery period, that an increase in food consumption was evident at the 500 and 1000 mg ai/kg diet levels.

Body Weight: Body weights were determined at study initiation (Week 1), every other week prior to the egg production period (Weeks 3, 5, 7, and 9), and at adult termination (Week 23). Male and female body weights were statistically analyzed at study initiation and termination; the study authors reported that all data were included in the statistical analysis, as the alterations to recovery replicates occurred only for the last 4 weeks of the study. No statistically-significant differences in body weight were observed at any level in males or females at study initiation or in males at study termination. However, compared to the control group at study termination (239 g), a statistically-significant increase in female body weights was observed at the 1000 mg ai/kg diet level (249 g) and a statistically-significant decrease in female body weights was observed at the 250 mg ai/kg diet level (221 g). It was reported that the increase in female body weight at the 1000 mg ai/kg diet level corresponded to very low egg production and increased food consumption at this level throughout the study.

Necropsy: All birds from the control, 250, and 1000 mg ai/kg diet levels and six birds per sex from the 500 mg ai/kg diet level (including the single decedent female) were necropsied. There were no indications of any treatment-related lesions or other findings. Several birds had feather loss and skin abrasions that were associated with cage wear and/or pen-mate aggression. The study authors reported that a high percentage of the females (i.e., ≥72%, reviewer-calculated) had maturing follicles for the control and all treatment groups, and that no lesions or growths were observed on the testes or ovaries for any of the birds.

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Reproductive Effects: During the first 5 weeks of the egg-laying period, when all replicates from all levels were fed treated diet, egg Lots A to F were produced. For the final 4 weeks of the egg-laying period, one-half of the replicates from the 500 and 1000 mg ai/kg diet levels (two highest levels) were offered untreated diet to assess their recovery potential, and the remainder of replicates as well as all birds from the 250 mg ai/kg diet level were maintained on treated diet for the duration of the study; egg Lots G to J were produced.

Profound treatment-related effects on reproduction were observed at all test levels compared to the control. Effects included reductions in the numbers of eggs laid, increases in the numbers of cracked or defective eggs, increases in embryonic mortality, reductions in egg shell strength and thickness, and reductions in the numbers of hatchlings and 14-day old survivors. In addition, the body weights of offspring and 14-day old survivors were inhibited 14-26% at the 500 and 1000 mg ai/kg diet levels compared to the controls.

The study authors reported that no abnormal symptoms were observed in hatchlings, and that the minor mortality observed in hatchlings occurred at all levels and did not follow dose-related trend.

Table 7: Reproductive and Other Parameters (nominal concentrations; study author-reported) for Egg Lots A to F (First 5 Weeks of Egg Laying Period).

Parameter	Control	250 mg/kg	500 mg/kg	1000 mg/kg	NOAEC/ LOAEC
Eggs laid	524	425*	276*	260*	<250 mg/kg 250 mg/kg
Eggs laid/hen/day	Parameter not assessed				N/A
Eggs cracked	6	27*	24*	16*	<250 mg/kg 250 mg/kg
Eggs cracked/eggs laid (%)	1	6	9	6	N/A
Eggs defective	3	62*	54*	40*	<250 mg/kg 250 mg/kg
Eggs defective/eggs laid (%)	1	15	20	15	N/A
Eggs set	476	301	173*	182*	<250 mg/kg 250 mg/kg
Shell thickness (mm ± SD)	0.192 ± 0.01	0.171* ± 0.02	0.170* ± 0.02	0.173* ± 0.02	<250 mg/kg 250 mg/kg
Shell strength (Kg ± SD)	0.86 ± 0.16	0.62* ± 0.20	0.52* ± 0.18	0.57* ± 0.20	<250 mg/kg 250 mg/kg
Viable embryos	452	245*	93*	103*	<250 mg/kg 250 mg/kg
Viable embryos/eggs set (%)	95	81	54	57	N/A
Live 18-day embryos	451	188*	66*	72*	<250 mg/kg 250 mg/kg

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Parameter	Control	250 mg/kg	500 mg/kg	1000 mg/kg	NOAEC/ LOAEC
Live 18-day embryos/viable embryos (%)	100	77	71	70	N/A
No. of hatchlings	431	159*	41*	7*	<250 mg/kg 250 mg/kg
No. of hatchlings/live 18-day embryos (%)	96	85	62	10	N/A
Hatchling weight (g ± SD)	6.5 ± 0.6	6.3 ± 0.6	5.6 ± 0.5	5.4 ± 0.6	N/A
14-day old survivors	427	159*	25*	3*	<250 mg/kg 250 mg/kg
14-day old survivors weight (g ± SD)	33.5 ± 3.3	30.4 ± 4.2	24.7 ± 4.6	28.2 (N/A)	N/A
14-day old survivors/hatchlings (%)	99	100	61	43	N/A
Mean food consumption (g/bird/day)	2.4	2.6	2.9	2.9	N/R
Weight (g) of parent females at test initiation: at onset of egg laying: at test termination:	189 202 239	189 198 221*(↓)	189 205 229	189 207 249*(↑)	N/R ^(a)
Weight (g) of parent males at test initiation: at onset of egg laying: at test termination:	192 201 219	194 202 219	195 209 219	196 208 220	N/R
Gross pathology	No treatment-related lesions observed.				N/R

N/A = Not statistically-analyzed.

N/R = Not reported.

^(a) It was reported that the increase in body weight of females at study termination corresponded to very low egg production and increased food consumption for this treatment throughout the study.

*Significantly different from the control at p≤0.05.

The study authors reported that positive results were observed for most reproductive endpoints during the 4-week recovery period (egg Lots G to J). For both the 500 and 1000 mg ai/kg diet levels, increases were observed in the numbers of eggs laid, eggs set, viable embryos, live 18-day embryos, hatchlings, and 14-day old survivors, and a decrease was observed in the number of cracked eggs. However, a decrease in the number of defective eggs and increases in hatchling and 14-day old survivor body weights were observed only at the 500 mg/kg diet level during the recovery period, but not at the 1000 mg ai/kg diet level. The study authors reported that the most dramatic improvement occurred for egg shell strength and thickness, where values obtained during recovery approached control levels.

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Table 8: Reproductive and Other Parameters (nominal concentrations; study author-reported) for Egg Lots G to J (Final 4 Weeks of Egg-Laying Period).

Parameter	Control	250 mg/kg	500 mg/kg		1000 mg/kg	
			Untreated	Treated	Untreated	Treated
Eggs laid	338	206	120	90	135	81
Eggs laid/hen/day	Parameter not assessed					
Eggs cracked	7	24	13	15	10	21
Eggs cracked/ eggs laid (%)	2	12	11	17	7	26
Eggs defective	2	24	5	18	11	6
Eggs defective/eggs laid (%)	1	12	4	20	8	7
Eggs set	310	142	92	49	107	49
Shell thickness (mm \pm SD)	0.197 \pm 0.011	0.174 \pm 0.018	0.194 \pm 0.010	0.176 \pm 0.010	0.193 \pm 0.012	0.186 \pm 0.044
Shell strength (Kg \pm SD)	0.85 \pm 0.14	0.63 \pm 0.16	0.84 \pm 0.08	0.46 \pm 0.09	0.83 \pm 0.27	0.83 \pm 0.21
Viable embryos	299	106	84	25	96	25
Viable embryos/eggs set (%)	96	75	91	51	90	51
Live 18-day embryos	299	83	81	10	95	19
Live 18-day embryos/viable embryos (%)	100	78	96	40	99	76
No. of hatchlings	277	69	74	4	88	0
No. of hatchlings/live 18-day embryos (%)	93	83	91	40	93	0
Hatchling weight (g \pm SD)	6.9 \pm 0.7	6.3 \pm 0.9	6.8 \pm 0.7	6.5 \pm 0.8	6.5 \pm 1.0	N/A
14-day old survivors	276	68	74	4	88	0
14-day old survivors weight (g \pm SD)	35.3 \pm 3.2	34.7 \pm 4.1	36.9 \pm 4.1	32.2 \pm 4.6	36.3 \pm 5.1	N/A
14-day old survivors/hatchlings (%)	99	99	100	100	100	0
Gross pathology	No treatment-related lesions observed					

N/A – Not applicable.

C. REPORTED STATISTICS:

The following parameters were statistically analyzed:

- Adult body weights for males and females at Weeks 1 and 23
- Overall average adult feed consumption through Week 19
- No. of eggs laid, eggs cracked, and eggs defective for egg Lots A to F
- Egg shell strength and thickness for egg Lots A to F
- No. of eggs set, viable embryos, and 18-day live embryos for egg Lots A to F
- No. of hatchlings and 14-day survivors for egg Lots A to F

Data were assessed for normality and homogeneity of variances using a Chi-Square Test and Bartlett's Test, respectively. If the data passed these assumptions, treatment groups were compared to the control group using an analysis of variance (ANOVA) followed by Bonferroni and/or Dunnett's tests. For data that was not homogeneous, a Kruskal Wallis Rank Test was performed.

It was reported that statistical analyses were not performed on the recovery portion of the study (egg Lots G to J) due to the study design and the nature of the data for the untreated replicates.

Analyses were conducted using ToxStat® statistical software (Version 3.4) at a 95% confidence level. Results were provided generally in terms of nominal concentrations.

III. REVIEWER'S EVALUATION:

A. DEVIATIONS FROM GUIDELINES

1. The initial age of the test birds (16 weeks) was younger than recommended (at least 30 weeks old).
2. Pre-test health (including mortality) of the adult birds was not reported.
3. Cage size was significantly smaller than recommended. OPPTS recommends at least 5,000 cm² per bird. In this study, the floor space was only 784 cm² per bird. Cage sizes smaller than recommended should be shown to not adversely affect the health or reproduction of the quail.
4. Temperature and humidity during hatching was not reported.
5. After only 5 weeks of egg-laying, the study design was modified to incorporate a recovery period. At this time, half of the 18 replicate pens from the 500 and 1000 mg ai/kg diet replicates were fed untreated feed for the final 4 weeks of the egg-laying period. Guidance requires that the (treated) egg-laying portion of the study last at least 8 weeks with at least 12 replicates per level.
6. Replicate data for offspring body weights (0 and 14 days) were not provided for the reviewer to statistically verify results for these endpoints.

B. OTHER STUDY DEFICIENCIES

Although not clearly specified, it appeared that offspring body weight data (0 and 14 days) as well as relative (percentage) reproductive data (e.g., percentage of eggs cracked of eggs laid, percentage of live embryos of viable embryos, percentage of 14-day survivors of embryos hatched) were not statistically analyzed by the study authors for egg Lots A to F (first 5 weeks of egg-laying period). Furthermore, no reproductive or offspring data were statistically analyzed by the study authors for egg Lots G to J (final 4 weeks of egg-laying period; includes recovery phase).

C. VERIFICATION OF STATISTICAL RESULTS:

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Statistical Method: Analysis was conducted using “chicks.sas” (Ver. 3; March 2002), a SAS program provided by EFED/OPP/USEPA. Data for all endpoints were examined graphically using box plots to determine if they exhibited a dose-dependent response, which was ultimately used to select the multiple comparison test to detect LOAEC and NOAEC. Data for each endpoint were tested to determine if their distributions were normal and if their variances were homogeneous using Shapiro-Wilk’s and Levene’s tests, respectively. Data that satisfied these assumptions were subjected to Dunnett’s and William’s tests and data that did not satisfy these assumptions were subjected to the non-parametric MannWhitney-U (with a Bonferroni adjustment) and Jonckheere’s tests. Data for dead birds were excluded from the analyses. See Appendix I for output of reviewer’s statistical verification and graphs for affected endpoints to support any reviewer-generated conclusions that may differ from those reported in the study. Only data during the exposure period was statistically analyzed by the reviewer. Due to the nature of the test design and presentation of replicate data during the recovery period, these data were not statistically analyzed by either the reviewer or the study authors.

NOAEC: <237 mg ai/kg

LOAEC: 237 mg ai/kg

Most Sensitive Endpoint(s): adult female body weight gain and all reproductive endpoints.

Table 9: Reproductive and Other Parameters- Initial 5-Week Egg Laying Period (mean-measured concentrations; reviewer-reported).

Parameter	Control	237 mg ai/kg	530 mg ai/kg	1082 mg ai/kg	NOAEC/ LOAEC
Eggs laid/pen	29.1	23.6	15.3***	14.4***	237 mg ai/kg 530 mg ai/kg
Eggs cracked/pen	0.3	1.5*	1.3*	0.9	<237 mg ai/kg 237 mg ai/kg
Eggs not cracked/eggs laid (%)	99.0	93.8***	93.5**	92.2*	<237 mg ai/kg 237 mg ai/kg
Eggs set/pen	26.4	16.7*	9.6***	10.1***	<237 mg ai/kg 237 mg ai/kg
Shell thickness	0.19	0.17**	0.17**	0.17**	<237 mg ai/kg 237 mg ai/kg
Eggs set/eggs laid (%)	91.4	69.7***	63.1***	70.1***	<237 mg ai/kg 237 mg ai/kg
Viable embryos/pen	25.1	13.6**	5.2***	5.7***	<237 mg ai/kg 237 mg ai/kg
Viable embryos/eggs set (%)	94.7	79.3***	54.5***	53.6***	<237 mg ai/kg 237 mg ai/kg
Live embryos/pen	25.1	10.4***	3.7***	4.0***	<237 mg ai/kg 237 mg ai/kg
Live embryos/viable embryos (%)	99.9	70.4***	69.2***	58.8***	<237 mg ai/kg 237 mg ai/kg

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No. of hatchlings/pen	23.9	8.8***	2.3***	0.4***	<237 mg ai/kg 237 mg ai/kg
No. of hatchlings/eggs laid (%)	83.2	33.7***	17.3***	3.8***	<237 mg ai/kg 237 mg ai/kg
No. of hatchlings/eggs set (%)	91.2	45.6***	27.1***	5.0***	<237 mg ai/kg 237 mg ai/kg
No. of hatchlings/live embryos (%)	96.4	78.0***	59.9***	17.7***	<237 mg ai/kg 237 mg ai/kg
Hatchling survival/pen	23.7	8.3***	1.4***	0.1***	<237 mg ai/kg 237 mg ai/kg
Hatchling survival/eggs set (%)	90.5	40.2***	17.7***	0.4***	<237 mg ai/kg 237 mg ai/kg
Hatchling survival/no. of hatchlings (%)	99.3	88.2*	46.7***	12.5***	<237 mg ai/kg 237 mg ai/kg
Hatchling weight (g)	NA	NA	NA	NA	NA
Survivor weight (g)	NA	NA	NA	NA	NA
Mean food consumption (g/bird/day)	268.6	275.8	276.1	290.7	1082 mg ai/kg >1082 mg ai/kg
Male weight gain (g)	27.7	25.8	25.0	25.2	1082 mg ai/kg >1082 mg ai/kg
Female weight gain (g)	50.4	32.1*	39.1	58.6	<237 mg ai/kg 237 mg ai/kg

* Statistically different from the control at p<0.05.

** Statistically different from the control at p<0.01.

*** Statistically different from the control at p<0.001.

NA=Not Analyzed; replicate data not provided for reviewer's verification.

D. ADDITIONAL REVIEWER COMMENTS:

With the exception of adult female weight gain, results of the reviewer's statistical verification were identical to the study authors'. Unlike the study authors' conclusion (that there were no adverse effects on adult parameters), the reviewer's analysis additionally detected a significant adverse effect on adult female weight gain at the lowest treatment level (237 mg ai/kg diet) during the first 5-week egg laying period. Mean-measured concentrations are reported in the Executive Summary and Conclusions sections of the DER.

All OPPTS 850.2300 validity requirements were met. Specifically, controls produced an average of 39 14-day old survivors per hen during the 9-week production phase (minimum of 12 quail per pen during a 10-week production phase), the egg shell thickness of control eggs averaged ≥ 0.192 mm (minimum of 0.19 mm for quail), and control mortality was 3% during the study (no more than 10% acceptable in controls).

The study authors reported that birds were from the same hatch, approaching their first breeding season, and had not

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been previously used in testing. Upon receipt, five birds per sex were necropsied to verify health, and a sub-sample of birds was swabbed for microbial examination. Swab samples were sent to the University of Missouri Veterinary Medical Diagnostic Laboratory (Columbia, MO). It was reported that no remarkable findings were observed either at necropsy or upon microbiological examination. All birds were examined daily during acclimation, and birds that exhibited abnormal behavior or injuries were excluded from the study. During acclimation, birds received 7 hours of light/day.

The basal ration contained at least 27% protein and 4% fat, and no more than 5% fiber. Offspring were fed basal ration without the addition of test substance.

Nominal concentrations were adjusted for the purity of the test substance. Concentration verification was performed on samples collected during Weeks 1, 5, 10, 15, and 20. Samples were stored frozen prior to analysis.

As significant treatment-related effects were observed on reproduction in the 250, 500, and 1000 mg ai/kg diet levels, the recovery potential was examined for the final 4 weeks of the study by providing clean untreated feed to half of the replicates in the 500 and 1000 mg ai/kg levels. Birds from the 250 mg ai/kg diet level and the other half of the replicates from the 500 and 1000 mg ai/kg diet levels continued to receive treated feed for the duration of the study. Comparisons were made with regard to treated versus untreated (i.e., recovery) replicates for reproductive and offspring endpoints.

Although the study authors referred to the duration of the egg-laying period prior to modification to include a recovery phase as 6 weeks, study dates and durations provided on page 14 of the study report clearly indicate that the total egg-laying period was 9 weeks (or 63 days), of which the final 4 weeks (29 days) incorporated the recovery period. Thus, the duration of the egg-laying period was actually 5 weeks prior to the recovery phase.

Stability was assessed in treated feed prepared at the 250 and 1000 mg ai/kg diet treatment levels after 12 weeks of frozen storage or after 10 days of ambient storage. After 12 weeks of frozen storage, recoveries were 93% of initial values for both concentrations. After 10 days of ambient storage, recoveries were 147 and 116% of initial values for the 250 and 1000 mg ai/kg diet levels, respectively. Fresh diets were offered weekly (on Tuesday) during the definitive study.

Homogeneity was assessed in treated feed prepared at the 250 and 1000 mg ai/kg diet levels following the initial mixing procedure. Nine samples per level were collected: three from the top, three from the middle, and three from the bottom of the batch. Calculated coefficients of variations (CV=RSD) were 6 and 9% for the 250 and 1000 mg ai/kg diet levels, respectively.

Treated feed samples were extracted by sonicating with acetonitrile for 20 minutes. An aliquot of the extract was filtered (0.45 µm) and diluted with acetonitrile (as needed) prior to analysis using HPLC with UV detection (220 nm). The LOQ for the procedure was 9.61 mg ai/kg diet. Untreated feed was fortified at 480 mg ai/kg diet and analyzed concurrently with the test samples. The mean recovery was 104% (range of 102-107%). It was not reported if sample results were corrected for mean procedural recoveries.

In an analytical method validation study (conducted October 12, 2006), samples of basal diet were spiked with AE C656948 at 9.61, 96.1, 480, or 961 mg ai/kg diet, extracted, and analyzed as described above for the definitive-study samples. The average recovery was 98% (range of 83 to 109%).

To prevent pathogen contamination, eggs were first washed in a Kuhl Egg Washer with warm water and a chlorine-based detergent, and then dipped into a solution of germicidal soap and warm water prior to cold storage.

For the first 4 days in the brooders, hatchling water was supplemented with Durvet brand water-soluble vitamin

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supplement (1 g/gal).

The study authors'-calculated daily dietary dosages were 23, 50, and 104 mg ai/kg bw/day for the 250, 500, and 1000 mg ai/kg diet levels, respectively.

The experimental dates were October 18, 2006 to April 24, 2007.

E. CONCLUSIONS:

This study is scientifically sound/unsound and is thus acceptable or unacceptable. Dietary exposure to AE C656948 (fluopyram) resulted in profound treatment-related effects on reproduction at all treatment levels. Additionally, the reviewer's analysis detected a significant adverse effect on adult female weight gain at the lowest treatment level, 237 mg ai/kg diet. During the recovery period, positive trends were observed at the 530 mg ai/kg diet level for all reproductive and hatchling endpoints (relative to the untreated birds during this period at this level), including egg production and quality, embryonic survival, and hatchling survival and body weights. At the 1082 mg ai/kg diet level, clear improvements on egg production and quality (excluding defective eggs), embryonic survival, and hatchling survival were observed (relative to untreated birds during this period at this level); however, hatchling body weights (0 and 14 days) did not show clear improvement.

NOAEC: <237 mg ai/kg diet

LOAEC: 237 mg ai/kg diet

Endpoint(s) Affected: adult female body weight gain and all reproductive and offspring endpoints

Most Sensitive Endpoint(s): adult female body weight gain and all reproductive and offspring endpoints

IV. REFERENCES:

- Organization for Economic Cooperation and Development. 1984. Avian Reproduction Test. OECD Guidelines for the Testing of Chemicals.
- U.S. Environmental Protection Agency. 1996. Ecological Effects Test Guidelines, OPPTS Number 850.2300: Avian Reproduction Test. Draft April 1996. Office of Prevention, Pesticides, and Toxic Substances.
- U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, subsection 71-4, Environmental Protection Agency, Office of Pesticide Programs. October 1982.
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- Sebaugh, J.L. 2004. Stratified randomization program. Sebaugh's Information Services, 3609 Holly Hills Court, Columbia, MO 65203, USA.
- Gulley, D.D. 1994. TOXSTAT® Version 3.4, Western EcoSystems Technology, Inc., Cheyenne, WY.

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APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:

Bobwhite repro, Fluopyram, MRID 47372345

PRINTOUT OF RAW DATA

Obs	TRT	EL	EC	ENC_EL	ES	ES_EL	VE	VE_ES	LE	LE_VE	NH	NH_EL	NH_ES
1	Ctrl	28	1	96.43	25	89.29	24	96.00	24	100.00	24	85.71	96.00
2	Ctrl	48	0	100.00	45	93.75	43	95.56	43	100.00	43	89.58	95.56
3	Ctrl	17	0	100.00	14	82.35	14	100.00	14	100.00	14	82.35	100.00
4	Ctrl	46	1	97.83	42	91.30	40	95.24	40	100.00	28	60.87	66.67
5	Ctrl	38	1	97.37	34	89.47	34	100.00	34	100.00	33	86.84	97.06
6	Ctrl	18	0	100.00	17	94.44	17	100.00	17	100.00	15	83.33	88.24
7	Ctrl	43	0	100.00	40	93.02	27	67.50	27	100.00	26	60.47	65.00
8	Ctrl	1	0	100.00	1	100.00	1	100.00	1	100.00	1	100.00	100.00
9	Ctrl	47	1	97.87	42	89.36	42	100.00	41	97.62	41	87.23	97.62
10	Ctrl	42	0	100.00	39	92.86	38	97.44	38	100.00	37	88.10	94.87
11	Ctrl	28	0	100.00	26	92.86	25	96.15	25	100.00	25	89.29	96.15
12	Ctrl	30	0	100.00	26	86.67	26	100.00	26	100.00	25	83.33	96.15
13	Ctrl	22	1	95.45	19	86.36	19	100.00	19	100.00	18	81.82	94.74
14	Ctrl	3	0	100.00	3	100.00	2	66.67	2	100.00	2	66.67	66.67
15	Ctrl	41	0	100.00	38	92.68	37	97.37	37	100.00	37	90.24	97.37
16	Ctrl	30	1	96.67	27	90.00	26	96.30	26	100.00	25	83.33	92.59
17	Ctrl	11	0	100.00	10	90.91	10	100.00	10	100.00	10	90.91	100.00
18	Ctrl	31	0	100.00	28	90.32	27	96.43	27	100.00	27	87.10	96.43
19	Dose1	14	1	92.86	8	57.14	7	87.50	4	57.14	0	0.00	0.00
20	Dose1	5	0	100.00	4	80.00	4	100.00	2	50.00	2	40.00	50.00
21	Dose1	21	1	95.24	6	28.57	5	83.33	5	100.00	4	19.05	66.67
22	Dose1	29	0	100.00	15	51.72	9	60.00	1	11.11	1	3.45	6.67
23	Dose1	28	2	92.86	21	75.00	19	90.48	16	84.21	12	42.86	57.14
24	Dose1	0	0	.	0	.	0	.	0	.	0	.	.
25	Dose1	30	0	100.00	26	86.67	25	96.15	19	76.00	16	53.33	61.54
26	Dose1	32	3	90.63	21	65.63	15	71.43	15	100.00	13	40.63	61.90
27	Dose1	16	0	100.00	15	93.75	11	73.33	6	54.55	5	31.25	33.33
28	Dose1	36	2	94.44	27	75.00	19	70.37	13	68.42	9	25.00	33.33
29	Dose1	24	2	91.67	18	75.00	7	38.89	7	100.00	7	29.17	38.89
30	Dose1	18	3	83.33	9	50.00	6	66.67	2	33.33	0	0.00	0.00
31	Dose1	22	2	90.91	16	72.73	14	87.50	6	42.86	5	22.73	31.25
32	Dose1	36	1	97.22	31	86.11	31	100.00	30	96.77	30	83.33	96.77
33	Dose1	20	0	100.00	17	85.00	12	70.59	11	91.67	10	50.00	58.82
34	Dose1	41	2	95.12	36	87.80	35	97.22	28	80.00	26	63.41	72.22
35	Dose1	25	4	84.00	10	40.00	6	60.00	3	50.00	3	12.00	30.00
36	Dose1	28	4	85.71	21	75.00	20	95.24	20	100.00	16	57.14	76.19
37	Dose2	16	1	93.75	9	56.25	7	77.78	4	57.14	4	25.00	44.44
38	Dose2	10	0	100.00	6	60.00	6	100.00	5	83.33	4	40.00	66.67
39	Dose2	13	2	84.62	7	53.85	6	85.71	5	83.33	4	30.77	57.14
40	Dose2	37	3	91.89	21	56.76	4	19.05	1	25.00	0	0.00	0.00
41	Dose2	1	0	100.00	1	100.00	0	0.00	0	.	0	0.00	0.00
42	Dose2	13	1	92.31	9	69.23	4	44.44	3	75.00	1	7.69	11.11
43	Dose2	18	3	83.33	9	50.00	2	22.22	1	50.00	1	5.56	11.11
44	Dose2	27	3	88.89	17	62.96	10	58.82	6	60.00	0	0.00	0.00
45	Dose2	13	0	100.00	12	92.31	9	75.00	7	77.78	3	23.08	25.00
46	Dose2	4	0	100.00	3	75.00	0	0.00	0	.	0	0.00	0.00
47	Dose2	26	5	80.77	13	50.00	5	38.46	2	40.00	1	3.85	7.69
48	Dose2	14	0	100.00	8	57.14	5	62.50	2	40.00	1	7.14	12.50
49	Dose2	4	0	100.00	3	75.00	3	100.00	3	100.00	3	75.00	100.00
50	Dose2	13	1	92.31	9	69.23	4	44.44	4	100.00	3	23.08	33.33

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51	Dose2	26	1	96.15	20	76.92	12	60.00	9	75.00	7	26.92	35.00
52	Dose2	16	2	87.50	8	50.00	7	87.50	5	71.43	1	6.25	12.50
53	Dose2	3	0	100.00	0	0.00	0	.	0	.	0	0.00	.
54	Dose2	22	2	90.91	18	81.82	9	50.00	9	100.00	8	36.36	44.44
55	Dose3	2	0	100.00	2	100.00	0	0.00	0	.	0	0.00	0.00
56	Dose3	3	0	100.00	3	100.00	2	66.67	1	50.00	1	33.33	33.33
57	Dose3	2	1	50.00	1	50.00	0	0.00	0	.	0	0.00	0.00
58	Dose3	14	2	85.71	10	71.43	3	30.00	1	33.33	0	0.00	0.00
59	Dose3	26	0	100.00	23	88.46	5	21.74	1	20.00	0	0.00	0.00
60	Dose3	23	3	86.96	15	65.22	8	53.33	5	62.50	2	8.70	13.33
61	Dose3	27	0	100.00	22	81.48	12	54.55	10	83.33	0	0.00	0.00
62	Dose3	0	0	.	0	.	0	.	0	.	0	.	.
63	Dose3	5	0	100.00	5	100.00	5	100.00	5	100.00	0	0.00	0.00
64	Dose3	16	0	100.00	15	93.75	14	93.33	11	78.57	0	0.00	0.00
65	Dose3	15	2	86.67	10	66.67	9	90.00	9	100.00	2	13.33	20.00
66	Dose3	29	2	93.10	18	62.07	15	83.33	14	93.33	0	0.00	0.00
67	Dose3	22	4	81.82	12	54.55	3	25.00	0	0.00	0	0.00	0.00
68	Dose3	21	0	100.00	15	71.43	12	80.00	10	83.33	0	0.00	0.00
69	Dose3	32	1	96.88	23	71.88	10	43.48	4	40.00	2	6.25	8.70
70	Dose3	0	0	.	0	.	0	.	0	.	0	.	.
71	Dose3	18	1	94.44	8	44.44	5	62.50	1	20.00	0	0.00	0.00
72	Dose3	5	0	100.00	0	0.00	0	.	0	.	0	0.00	.

Bobwhite repro, Fluopyram, MRID 47372345

PRINTOUT OF RAW DATA (continued)

Obs	TRT	NH_LE	HS	HS_ES	HS_NH	THICK	HATWT	SURVWT	FOOD	WTGAINM	WTGAINF
1	Ctrl	100.00	24	96.00	100.00	0.20	.	.	230	55	55
2	Ctrl	100.00	43	95.56	100.00	0.19	.	.	270	34	21
3	Ctrl	100.00	14	100.00	100.00	0.21	.	.	243	58	48
4	Ctrl	70.00	28	66.67	100.00	0.20	.	.	265	19	57
5	Ctrl	97.06	33	97.06	100.00	0.19	.	.	296	24	107
6	Ctrl	88.24	15	88.24	100.00	0.20	.	.	273	19	43
7	Ctrl	96.30	26	65.00	100.00	0.21	.	.	246	37	59
8	Ctrl	100.00	1	100.00	100.00	.	.	.	273	20	41
9	Ctrl	100.00	41	97.62	100.00	0.19	.	.	306	24	60
10	Ctrl	97.37	36	92.31	97.30	0.19	.	.	237	24	64
11	Ctrl	100.00	23	88.46	92.00	0.20	.	.	246	6	54
12	Ctrl	96.15	25	96.15	100.00	0.18	.	.	302	18	63
13	Ctrl	94.74	18	94.74	100.00	0.20	.	.	255	39	37
14	Ctrl	100.00	2	66.67	100.00	.	.	.	234	.	.
15	Ctrl	100.00	36	94.74	97.30	0.18	.	.	325	44	39
16	Ctrl	96.15	25	92.59	100.00	0.17	.	.	299	2	47
17	Ctrl	100.00	10	100.00	100.00	0.18	.	.	204	45	-10
18	Ctrl	100.00	27	96.43	100.00	0.19	.	.	331	3	72
19	Dose1	0.00	0	0.00	.	0.17	.	.	239	.	.
20	Dose1	100.00	0	0.00	0.00	.	.	.	254	13	64
21	Dose1	80.00	3	50.00	75.00	0.18	.	.	254	18	40
22	Dose1	100.00	1	6.67	100.00	0.18	.	.	287	29	16
23	Dose1	75.00	12	57.14	100.00	0.16	.	.	330	52	17
24	Dose1	.	0	239	.	.
25	Dose1	84.21	16	61.54	100.00	0.19	.	.	316	33	31
26	Dose1	86.67	12	57.14	92.31	0.14	.	.	253	23	43
27	Dose1	83.33	5	33.33	100.00	0.17	.	.	274	35	38
28	Dose1	69.23	6	22.22	66.67	0.18	.	.	310	14	17
29	Dose1	100.00	7	38.89	100.00	0.18	.	.	218	14	19

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

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30	Dose1	0.00	0	0.00	266	31	49
31	Dose1	83.33	5	31.25	100.00	0.14	.	.	322	32	26
32	Dose1	100.00	29	93.55	96.67	0.17	.	.	301	19	12
33	Dose1	90.91	10	58.82	100.00	0.19	.	.	288	21	33
34	Dose1	92.86	24	66.67	92.31	0.16	.	.	258	37	73
35	Dose1	100.00	3	30.00	100.00	0.15	.	.	338	7	48
36	Dose1	80.00	16	76.19	100.00	0.21	.	.	218	34	-13
37	Dose2	100.00	0	0.00	0.00	.	.	.	225	25	23
38	Dose2	80.00	4	66.67	100.00	0.17	.	.	254	16	29
39	Dose2	80.00	2	28.57	50.00	0.20	.	.	236	23	-8
40	Dose2	0.00	0	0.00	.	0.13	.	.	256	19	66
41	Dose2	.	0	0.00	240	14	68
42	Dose2	33.33	0	0.00	0.00	0.19	.	.	286	31	-10
43	Dose2	100.00	1	11.11	100.00	0.19	.	.	211	21	48
44	Dose2	0.00	0	0.00	.	0.17	.	.	275	38	42
45	Dose2	42.86	1	8.33	33.33	0.15	.	.	264	40	67
46	Dose2	.	0	0.00	.	0.15	.	.	236	42	6
47	Dose2	50.00	0	0.00	0.00	0.13	.	.	290	15	35
48	Dose2	50.00	0	0.00	0.00	0.18	.	.	300	43	76
49	Dose2	100.00	3	100.00	100.00	.	.	.	389	10	48
50	Dose2	75.00	2	22.22	66.67	.	.	.	340	29	5
51	Dose2	77.78	4	20.00	57.14	0.18	.	.	314	17	60
52	Dose2	20.00	0	0.00	0.00	0.17	.	.	278	30	59
53	Dose2	.	0	305	.	.
54	Dose2	88.89	8	44.44	100.00	0.21	.	.	271	12	51
55	Dose3	.	0	0.00	315	-23	62
56	Dose3	100.00	0	0.00	0.00	.	.	.	314	38	62
57	Dose3	.	0	0.00	278	37	49
58	Dose3	0.00	0	0.00	.	0.18	.	.	228	43	58
59	Dose3	0.00	0	0.00	.	0.16	.	.	317	43	70
60	Dose3	40.00	1	6.67	50.00	0.18	.	.	291	24	59
61	Dose3	0.00	0	0.00	.	0.20	.	.	231	39	51
62	Dose3	.	0	244	.	.
63	Dose3	0.00	0	0.00	273	16	56
64	Dose3	0.00	0	0.00	.	0.20	.	.	293	22	67
65	Dose3	22.22	0	0.00	0.00	0.14	.	.	278	20	65
66	Dose3	0.00	0	0.00	.	0.14	.	.	283	.	.
67	Dose3	.	0	0.00	.	0.18	.	.	368	38	63
68	Dose3	0.00	0	0.00	288	18	34
69	Dose3	50.00	0	0.00	0.00	0.19	.	.	391	36	62
70	Dose3	.	0	270	-1	53
71	Dose3	0.00	0	0.00	.	0.14	.	.	325	43	75
72	Dose3	.	0	246	11	52

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

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EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345
ANALYSIS RESULTS FOR VARIABLE EL (Eggs Laid)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.980	0.311	1.499	0.223	USE PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	29.11	14.69	3.46	50.47	21.80, 36.42
Dose1	18	23.61	10.57	2.49	44.75	18.36, 28.87
Dose2	18	15.33	9.55	2.25	62.31	10.58, 20.08
Dose3	18	14.44	10.94	2.58	75.77	9.00, 19.89

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	30.00	1.00	48.00	.	.
Dose1	24.50	0.00	41.00	81.11	18.89
Dose2	13.50	1.00	37.00	52.67	47.33
Dose3	15.50	0.00	32.00	49.62	50.38

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
3	68	6.56	<.001

Dunnett - testing each trt mean signif. less than control

Williams - test assumes dose-response relationship, testing negative trend

Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	29.11	.	29.11	.	0.490	0.004	0.002	.	.
Dose1	23.61	0.179	23.61	0.094	.	0.151	0.093	.	.
Dose2	15.33	<.001	15.33	<.001	.	.	0.996	.	.
Dose3	14.44	<.001	14.44	<.001

SUMMARY

Dunnett

Williams

NOEC

Dose1

Dose1

LOEC

Dose2

Dose2

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE NEG_EC (Eggs Cracked)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.920	<.001	5.353	0.002	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	0.33	0.49	0.11	145.52	0.09, 0.57
Dose1	18	1.50	1.38	0.33	92.18	0.81, 2.19
Dose2	18	1.33	1.46	0.34	109.14	0.61, 2.06
Dose3	18	0.89	1.23	0.29	138.53	0.28, 1.50

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	0.00	0.00	1.00	.	.
Dose1	1.50	0.00	4.00	450.00	-350.00
Dose2	1.00	0.00	5.00	400.00	-300.00
Dose3	0.00	0.00	4.00	266.67	-166.67

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	8.70	0.033

MannWhit(Bon) - testing each trt median signif. greater than control

Jonckheere - test assumes dose-response relationship, testing positive trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	0.00	.	.
Dose1	1.50	0.014	0.003
Dose2	1.00	0.044	0.012
Dose3	0.00	1.000	0.156

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	Dose3	>highest dose

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE ENC_EL ((EL-EC)/EL (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.766	<.001	6.206	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	98.98	1.57	0.37	1.59	98.20, 99.76
Dose1	17	93.76	5.61	1.36	5.98	90.88, 96.65
Dose2	18	93.47	6.49	1.53	6.95	90.24, 96.70
Dose3	16	92.22	12.92	3.23	14.01	85.34, 99.11

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	95.45	100.00	.	.
Dose1	94.44	83.33	100.00	94.73	5.27
Dose2	93.03	80.77	100.00	94.43	5.57
Dose3	98.44	50.00	100.00	93.18	6.82

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	9.97	0.019

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	100.00	.	.
Dose1	94.44	0.005	<.001
Dose2	93.03	0.019	0.002
Dose3	98.44	0.142	0.018

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345
ANALYSIS RESULTS FOR VARIABLE ES (Eggs Set)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.982	0.402	3.508	0.020	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	26.44	13.57	3.20	51.33	19.69, 33.19
Dose1	18	16.72	9.60	2.26	57.42	11.95, 21.50
Dose2	18	9.61	6.23	1.47	64.84	6.51, 12.71
Dose3	18	10.11	8.22	1.94	81.27	6.02, 14.20

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	26.50	1.00	45.00	.	.
Dose1	16.50	0.00	36.00	63.24	36.76
Dose2	9.00	0.00	21.00	36.34	63.66
Dose3	10.00	0.00	23.00	38.24	61.76

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	20.14	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	26.50	.	.
Dose1	16.50	0.046	0.012
Dose2	9.00	0.001	<.001
Dose3	10.00	0.002	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE ES_EL (EggsSet/EggsLaid (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.909	<.001	4.949	0.004	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	91.43	4.32	1.02	4.72	89.28, 93.57
Dose1	17	69.71	18.34	4.45	26.31	60.28, 79.14
Dose2	18	63.14	21.46	5.06	33.99	52.47, 73.81
Dose3	16	70.09	25.86	6.47	36.90	56.30, 83.87

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	91.11	82.35	100.00	.	.
Dose1	75.00	28.57	93.75	76.25	23.75
Dose2	61.48	0.00	100.00	69.06	30.94
Dose3	71.43	0.00	100.00	76.66	23.34

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	23.33	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	91.11	.	.
Dose1	75.00	<.001	<.001
Dose2	61.48	<.001	<.001
Dose3	71.43	0.021	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE VE (Viable Embryo(d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.971	0.098	7.253	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	25.11	12.82	3.02	51.05	18.74, 31.49
Dose1	18	13.61	9.63	2.27	70.75	8.82, 18.40
Dose2	18	5.17	3.49	0.82	67.46	3.43, 6.90
Dose3	18	5.72	5.21	1.23	91.06	3.13, 8.31

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	26.00	1.00	43.00	.	.
Dose1	11.50	0.00	35.00	54.20	45.80
Dose2	5.00	0.00	12.00	20.58	79.42
Dose3	5.00	0.00	15.00	22.79	77.21

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	29.02	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	26.00	.	.
Dose1	11.50	0.017	0.004
Dose2	5.00	<.001	<.001
Dose3	5.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE VE_ES (ViableEmbryo/EggsSet (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.961	0.034	8.933	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	94.70	10.22	2.41	10.79	89.62, 99.78
Dose1	17	79.34	17.29	4.19	21.79	70.45, 88.22
Dose2	17	54.47	31.62	7.67	58.05	38.21, 70.72
Dose3	15	53.60	32.87	8.49	61.33	35.39, 71.80

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	97.40	66.67	100.00	.	.
Dose1	83.33	38.89	100.00	83.77	16.23
Dose2	58.82	0.00	100.00	57.51	42.49
Dose3	54.55	0.00	100.00	56.59	43.41

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	26.32	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	97.40	.	.
Dose1	83.33	0.006	0.001
Dose2	58.82	<.001	<.001
Dose3	54.55	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE LE (Live Embryo(d21))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.959	0.020	9.133	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	25.06	12.74	3.00	50.86	18.72, 31.39
Dose1	18	10.44	9.18	2.16	87.89	5.88, 15.01
Dose2	18	3.67	2.87	0.68	78.27	2.24, 5.09
Dose3	18	4.00	4.73	1.11	118.20	1.65, 6.35

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	26.00	1.00	43.00	.	.
Dose1	6.50	0.00	30.00	41.69	58.31
Dose2	3.50	0.00	9.00	14.63	85.37
Dose3	1.00	0.00	14.00	15.96	84.04

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	30.29	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	26.00	.	.
Dose1	6.50	0.006	0.001
Dose2	3.50	<.001	<.001
Dose3	1.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE LE_VE (LiveEmbryo/ViableEmbryo (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.954	0.021	19.311	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	99.87	0.56	0.13	0.56	99.59, 100.00
Dose1	17	70.36	27.25	6.61	38.73	56.35, 84.37
Dose2	15	69.20	23.37	6.04	33.78	56.26, 82.15
Dose3	13	58.80	33.84	9.39	57.55	38.35, 79.25

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	97.62	100.00	.	.
Dose1	76.00	11.11	100.00	70.45	29.55
Dose2	75.00	25.00	100.00	69.29	30.71
Dose3	62.50	0.00	100.00	58.88	41.12

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	26.13	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	100.00	.	.
Dose1	76.00	<.001	<.001
Dose2	75.00	<.001	<.001
Dose3	62.50	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE NH (Number Hatched)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.897	<.001	13.772	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	23.94	12.19	2.87	50.92	17.88, 30.01
Dose1	18	8.83	8.77	2.07	99.24	4.47, 13.19
Dose2	18	2.28	2.42	0.57	106.27	1.07, 3.48
Dose3	18	0.39	0.78	0.18	199.94	0.00, 0.78

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	25.00	1.00	43.00	.	.
Dose1	6.00	0.00	30.00	36.89	63.11
Dose2	1.00	0.00	8.00	9.51	90.49
Dose3	0.00	0.00	2.00	1.62	98.38

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	43.28	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	25.00	.	.
Dose1	6.00	0.003	<.001
Dose2	1.00	<.001	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE NH_EL (NumberHatched/EggsLaid (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.947	0.006	7.058	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	83.18	10.39	2.45	12.49	78.01, 88.34
Dose1	17	33.73	23.47	5.69	69.59	21.66, 45.79
Dose2	18	17.26	19.91	4.69	115.36	7.36, 27.16
Dose3	16	3.85	8.82	2.20	228.99	0.00, 8.55

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	86.28	60.47	100.00	.	.
Dose1	31.25	0.00	83.33	40.55	59.45
Dose2	7.42	0.00	75.00	20.75	79.25
Dose3	0.00	0.00	33.33	4.63	95.37

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	47.91	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	86.28	.	.
Dose1	31.25	<.001	<.001
Dose2	7.42	<.001	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE NH_ES (NumberHatched/EggsSet (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.961	0.035	7.988	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	91.17	11.86	2.80	13.01	85.27, 97.07
Dose1	17	45.57	27.41	6.65	60.15	31.48, 59.67
Dose2	17	27.11	28.22	6.84	104.08	12.61, 41.62
Dose3	15	5.02	9.95	2.57	198.03	0.00, 10.53

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	96.08	65.00	100.00	.	.
Dose1	50.00	0.00	96.77	49.99	50.01
Dose2	12.50	0.00	100.00	29.74	70.26
Dose3	0.00	0.00	33.33	5.51	94.49

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	43.31	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	96.08	.	.
Dose1	50.00	<.001	<.001
Dose2	12.50	<.001	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE NH_LE (NumberHatched/LiveEmbryo (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.920	<.001	6.705	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	96.44	7.27	1.71	7.53	92.83, 100.00
Dose1	17	77.97	30.86	7.49	39.58	62.10, 93.84
Dose2	15	59.86	34.83	8.99	58.18	40.57, 79.14
Dose3	12	17.69	31.39	9.06	177.51	0.00, 37.63

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	70.00	100.00	.	.
Dose1	84.21	0.00	100.00	80.85	19.15
Dose2	75.00	0.00	100.00	62.06	37.94
Dose3	0.00	0.00	100.00	18.34	81.66

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	27.13	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	100.00	.	.
Dose1	84.21	0.019	0.004
Dose2	75.00	0.003	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE HS (Hatching Survival(d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.885	<.001	16.234	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	23.72	12.07	2.84	50.87	17.72, 29.72
Dose1	18	8.28	8.53	2.01	103.08	4.03, 12.52
Dose2	18	1.39	2.17	0.51	156.46	0.31, 2.47
Dose3	18	0.06	0.24	0.06	424.26	0.00, 0.17

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	25.00	1.00	43.00	.	.
Dose1	5.50	0.00	29.00	34.89	65.11
Dose2	0.00	0.00	8.00	5.85	94.15
Dose3	0.00	0.00	1.00	0.23	99.77

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	47.35	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	25.00	.	.
Dose1	5.50	0.002	<.001
Dose2	0.00	<.001	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE HS_ES (HatchingSurvival/EggsSet (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Test Stat	Shapiro-Wilks P-value	Levenes Test Stat	Levenes P-value	Conclusion
0.906	<.001	11.066	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	90.46	11.70	2.76	12.93	84.64, 96.27
Dose1	17	40.20	28.33	6.87	70.48	25.63, 54.77
Dose2	17	17.73	28.48	6.91	160.68	3.08, 32.37
Dose3	15	0.44	1.72	0.44	387.30	0.00, 1.40

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	95.15	65.00	100.00	.	.
Dose1	38.89	0.00	93.55	44.44	55.56
Dose2	0.00	0.00	100.00	19.60	80.40
Dose3	0.00	0.00	6.67	0.49	99.51

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	46.04	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	95.15	.	.
Dose1	38.89	<.001	<.001
Dose2	0.00	<.001	<.001
Dose3	0.00	<.001	<.001

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	<lowest dose	Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE HS_NH (HatchingSurvival/NumberHatched (%))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.871	<.001	14.954	<.001	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	99.26	2.01	0.47	2.02	98.26, 100.00
Dose1	15	88.20	26.42	6.82	29.96	73.56, 100.00
Dose2	13	46.70	43.75	12.13	93.67	20.27, 73.14
Dose3	4	12.50	25.00	12.50	200.00	0.00, 52.28

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	100.00	92.00	100.00	.	.
Dose1	100.00	0.00	100.00	88.86	11.14
Dose2	50.00	0.00	100.00	47.05	52.95
Dose3	0.00	0.00	50.00	12.59	87.41

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	21.30	<.001

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	100.00	.	.
Dose1	100.00	1.000	0.042
Dose2	50.00	0.003	<.001
Dose3	0.00	0.002	<.001

SUMMARY

MannWhit (Bonf adjust)

Jonckheere

NOEC

Dose1

<lowest dose

LOEC

Dose2

Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE THICK (Eggshell thickness)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.982	0.585	2.610	0.062	USE PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	16	0.19	0.01	0.00	5.77	0.19, 0.20
Dose1	15	0.17	0.02	0.01	11.69	0.16, 0.18
Dose2	13	0.17	0.03	0.01	14.73	0.15, 0.19
Dose3	10	0.17	0.02	0.01	13.85	0.15, 0.19

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	0.19	0.17	0.21	.	.
Dose1	0.17	0.14	0.21	89.24	10.76
Dose2	0.17	0.13	0.21	88.54	11.46
Dose3	0.18	0.14	0.20	88.65	11.35

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
3	50	4.32	0.009

Dunnett - testing each trt mean signif. less than control

Williams - test assumes dose-response relationship, testing negative trend

Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	0.19	.	0.19	.	0.029	0.024	0.045	.	.
Dose1	0.17	0.008	0.17	0.003	.	0.998	0.999	.	.
Dose2	0.17	0.007	0.17	0.003	.	.	1.000	.	.
Dose3	0.17	0.013	0.17	0.005

SUMMARY

Dunnett

Williams

NOEC

<lowest dose

<lowest dose

LOEC

Dose1

Dose1

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE HATWT (Hatchling Weight)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
.	.	.	.	NO DATA FOR TEST

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	0
Dose1	0
Dose2	0
Dose3	0

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl
Dose1
Dose2
Dose3

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE SURVWT (Survivor Wt (d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
.	.	.	.	NO DATA FOR TEST

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	0
Dose1	0
Dose2	0
Dose3	0

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl
Dose1
Dose2
Dose3

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE FOOD (Food Consumption)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.972	0.108	0.100	0.960	USE PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	18	268.61	35.18	8.29	13.10	251.12, 286.11
Dose1	18	275.83	37.50	8.84	13.60	257.18, 294.48
Dose2	18	276.11	43.66	10.29	15.81	254.40, 297.82
Dose3	18	290.72	43.28	10.20	14.89	269.20, 312.25

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	267.50	204.00	331.00	.	.
Dose1	270.00	218.00	338.00	102.69	-2.69
Dose2	273.00	211.00	389.00	102.79	-2.79
Dose3	285.50	228.00	391.00	108.23	-8.23

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
3	68	0.96	0.415

Dunnett - testing each trt mean signif. less than control

Williams - test assumes dose-response relationship, testing negative trend

Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-values Dose3	Dose4	Dose5
Ctrl	268.61	.	277.82	.	0.949	0.943	0.355	.	.
Dose1	275.83	0.902	277.82	0.834	.	1.000	0.682	.	.
Dose2	276.11	0.906	277.82	0.863	.	.	0.694	.	.
Dose3	290.72	0.995	277.82	0.877

SUMMARY

	NOEC	LOEC
Dunnett	Dose3	>highest dose
Williams	Dose3	>highest dose

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE WTGAINM (Male wt gain)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.972	0.145	1.877	0.143	USE PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	17	27.71	16.90	4.10	61.00	19.02, 36.39
Dose1	16	25.75	11.62	2.90	45.12	19.56, 31.94
Dose2	17	25.00	10.90	2.64	43.59	19.40, 30.60
Dose3	16	25.25	18.46	4.61	73.10	15.41, 35.09

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	24.00	2.00	58.00	.	.
Dose1	26.00	7.00	52.00	92.94	7.06
Dose2	23.00	10.00	43.00	90.23	9.77
Dose3	30.00	-23.00	43.00	91.14	8.86

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df	Denominator df	F-stat	P-value
3	62	0.12	0.951

Dunnett - testing each trt mean signif. less than control

Williams - test assumes dose-response relationship, testing negative trend

Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-values		
							Dose3	Dose4	Dose5
Ctrl	27.71	.	27.71	.	0.981	0.951	0.964	.	.
Dose1	25.75	0.599	25.75	0.419	.	0.999	1.000	.	.
Dose2	25.00	0.530	25.12	0.390	.	.	1.000	.	.
Dose3	25.25	0.556	25.12	0.408

SUMMARY

Dunnett	NOEC	LOEC
Williams	Dose3	>highest dose
	Dose3	>highest dose

Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

EPA MRID Number 473723-45

Bobwhite repro, Fluopyram, MRID 47372345

ANALYSIS RESULTS FOR VARIABLE WTGAINF (Female wt gain)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05

Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.973	0.162	3.773	0.015	USE NON-PARAMETRIC TESTS

BASIC SUMMARY STATISTICS

Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval
Ctrl	17	50.41	24.03	5.83	47.67	38.06, 62.77
Dose1	16	32.06	21.31	5.33	66.45	20.71, 43.42
Dose2	17	39.12	27.51	6.67	70.32	24.98, 53.26
Dose3	16	58.63	9.67	2.42	16.49	53.47, 63.78

Level	Median	Min	Max	%of Control(means)	%Reduction(means)
Ctrl	54.00	-10.00	107.00	.	.
Dose1	32.00	-13.00	73.00	63.60	36.40
Dose2	48.00	-10.00	76.00	77.60	22.40
Dose3	60.50	34.00	75.00	116.29	-16.29

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom	TestStat	P-value
3	13.50	0.004

MannWhit(Bon) - testing each trt median signif. less than control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	54.00	.	.
Dose1	32.00	0.035	0.008
Dose2	48.00	0.696	0.145
Dose3	60.50	1.000	0.942

SUMMARY

	NOEC	LOEC
MannWhit (Bonf adjust)	<lowest dose	Dose1
Jonckheere	Dose3	>highest dose

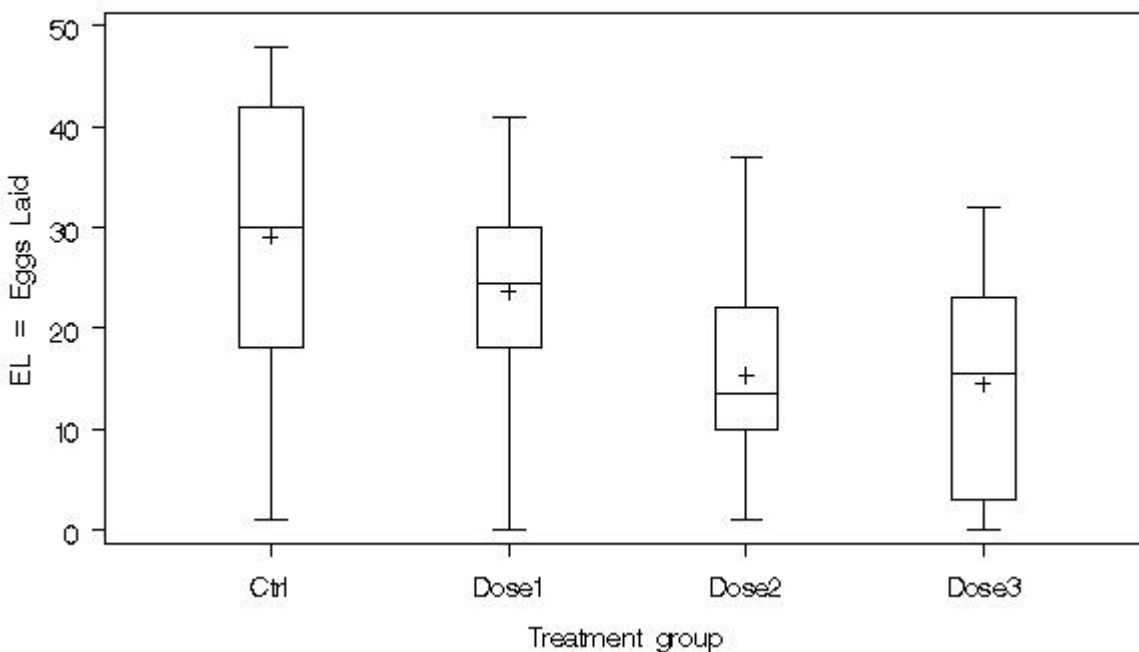
Data Summary and Review on the Reproductive Effects of AE C656948 (Fluopyram) on Northern Bobwhite (*Colinus virginianus*)

PMRA Submission Number {.....}

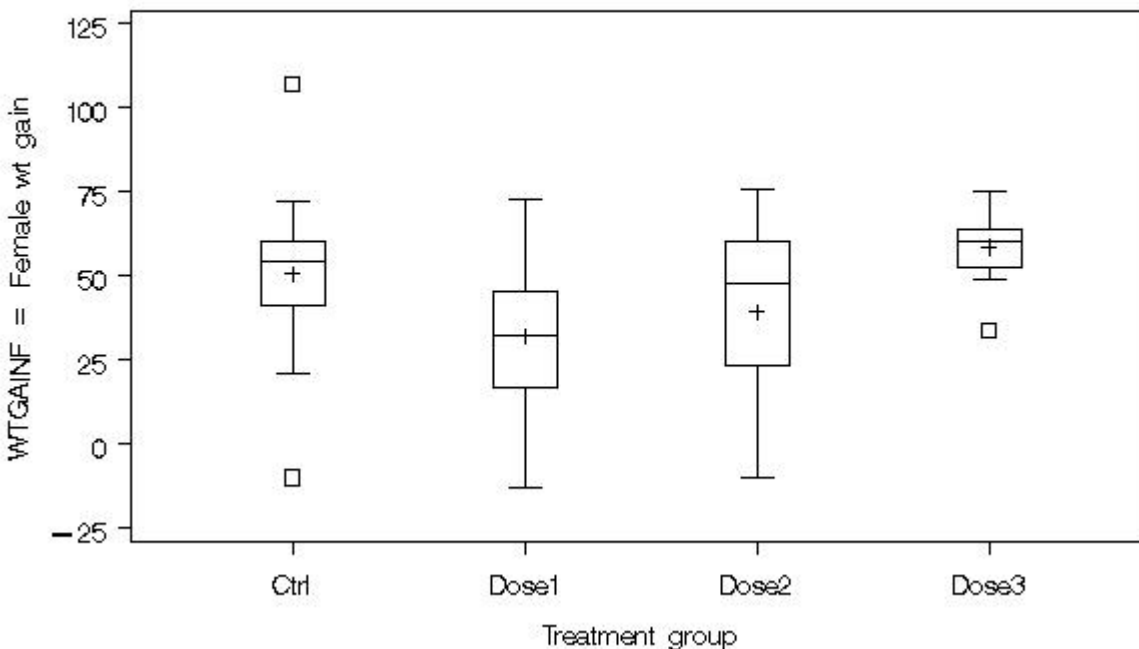
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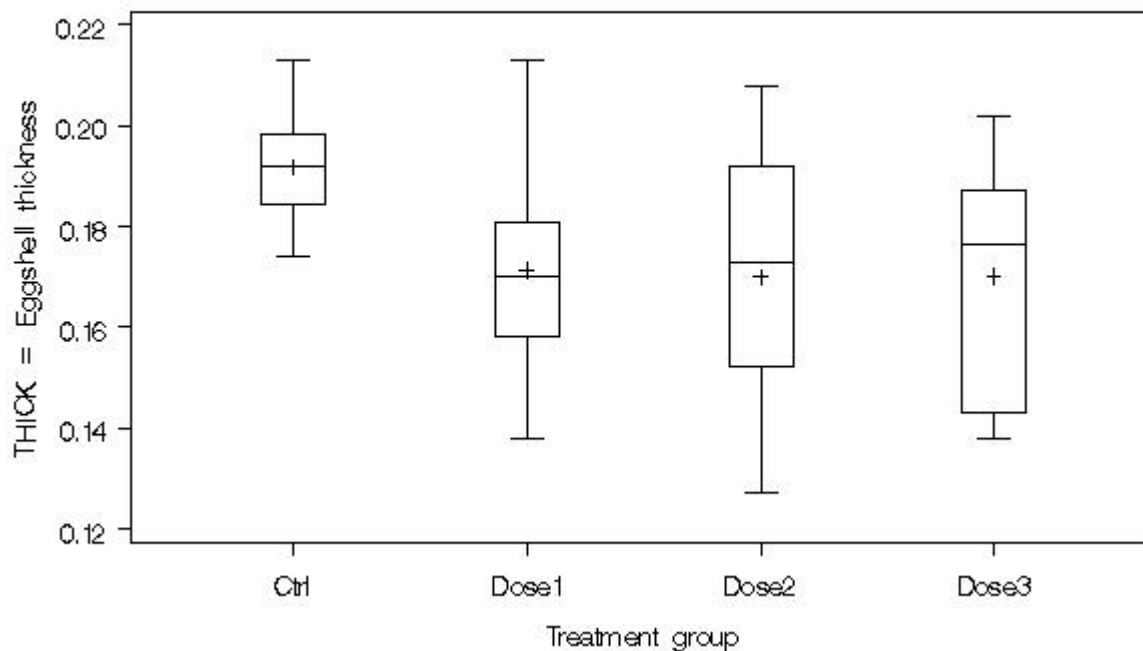
Bobwhite repro, Fluopyram, MRID 47372345



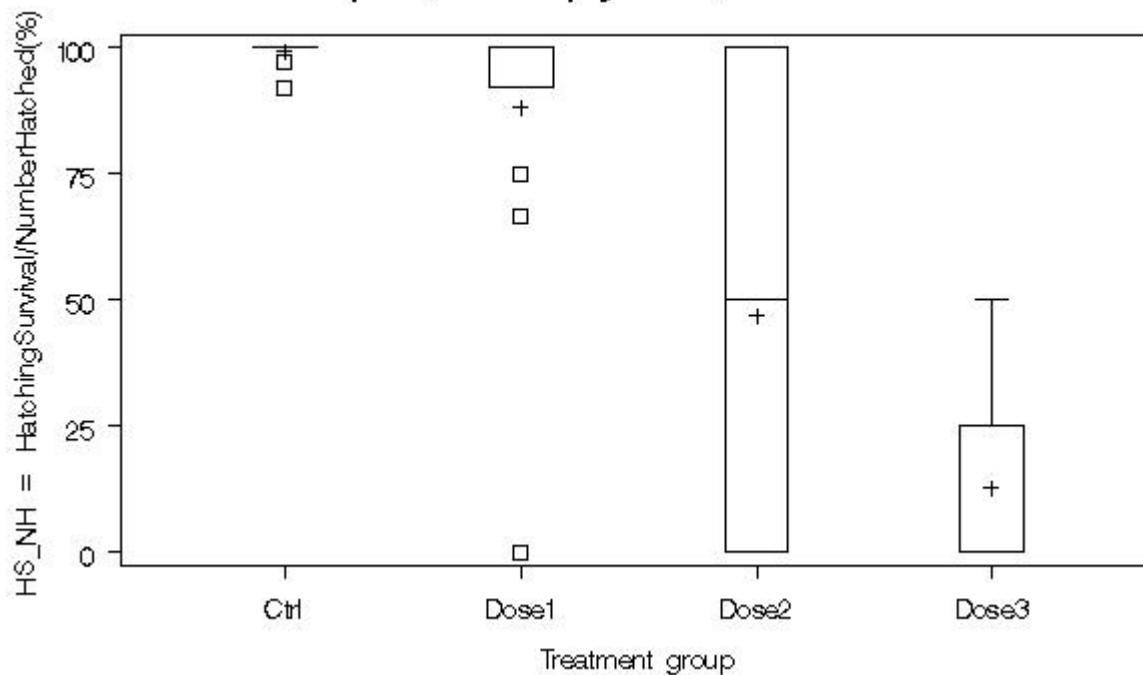
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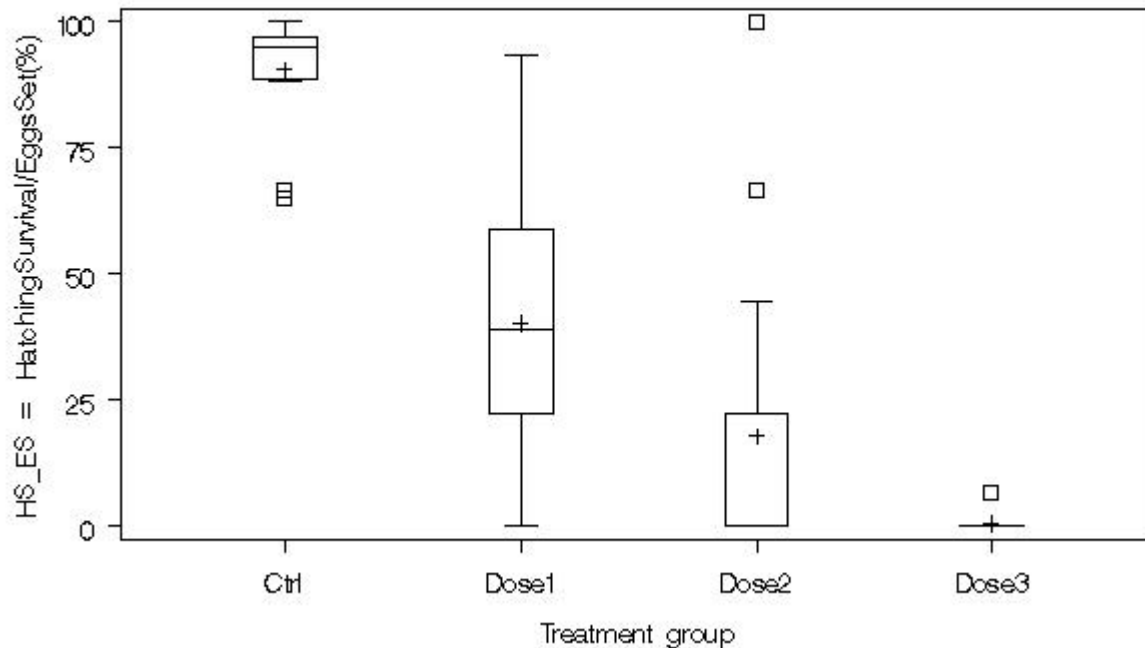
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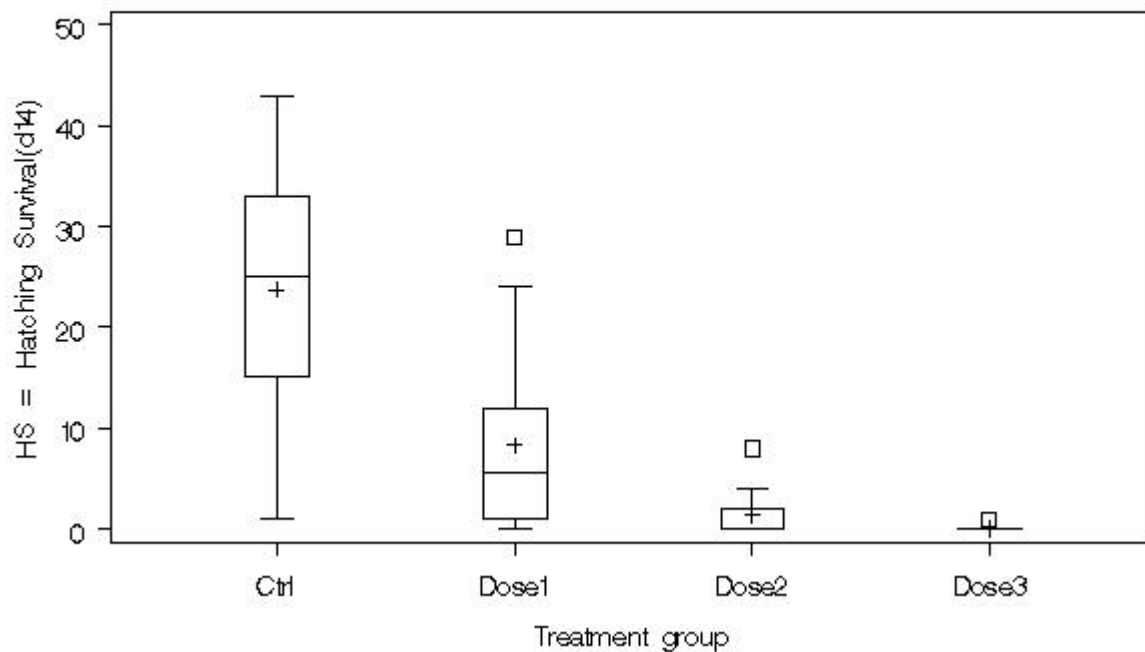
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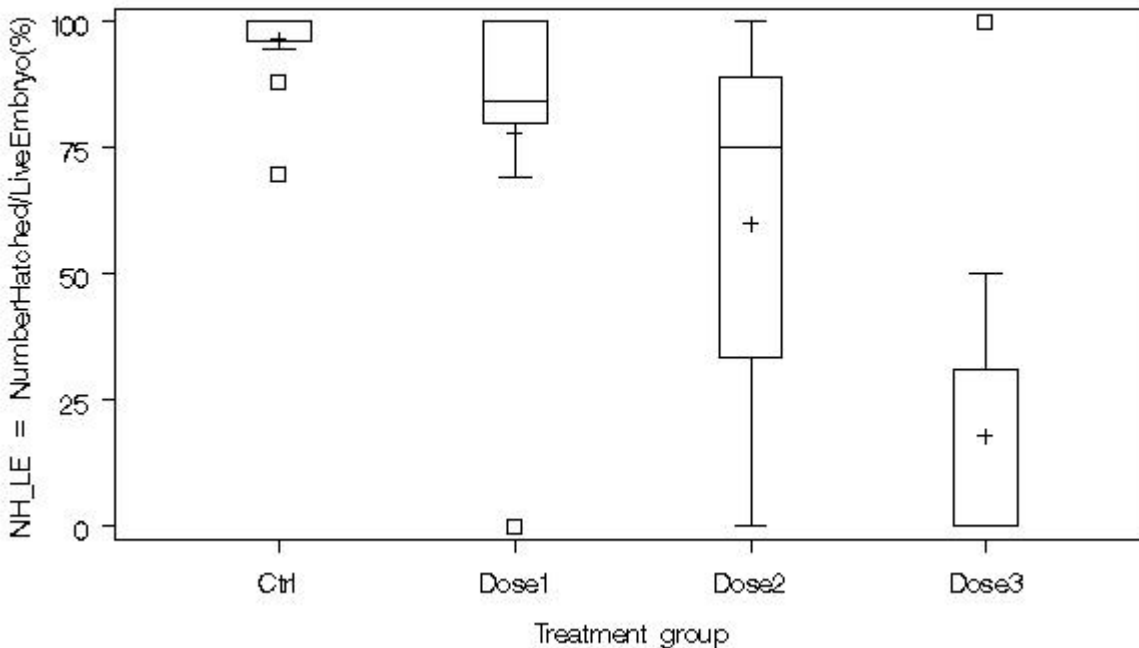
Bobwhite repro, Fluopyram, MRID 47372345



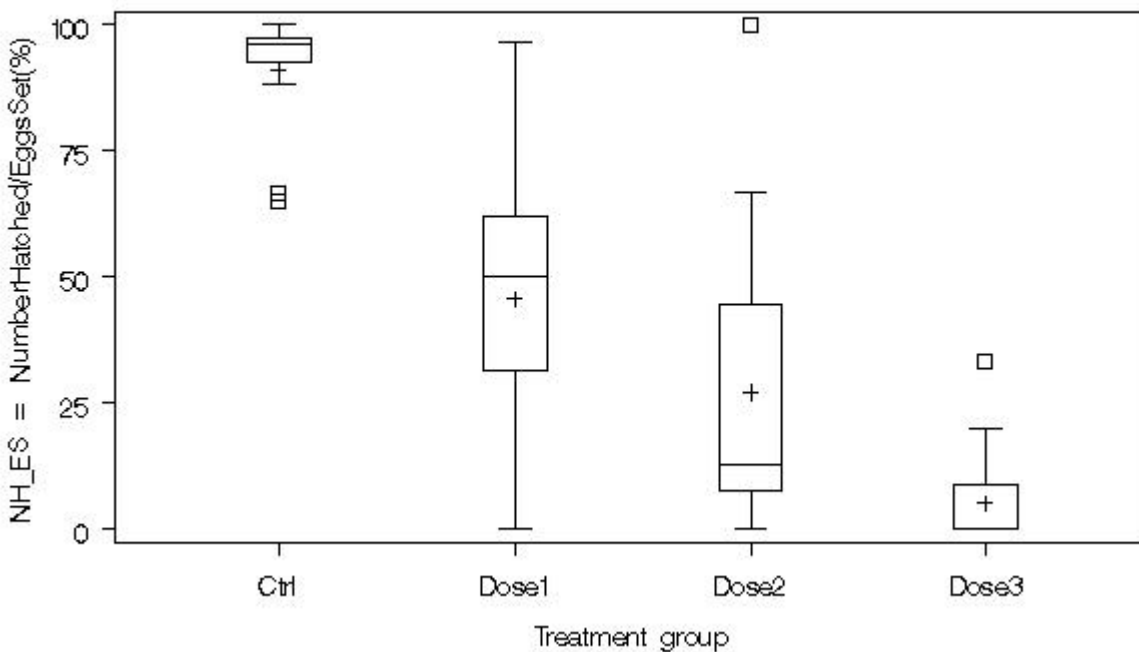
Bobwhite repro, Fluopyram, MRID 47372345



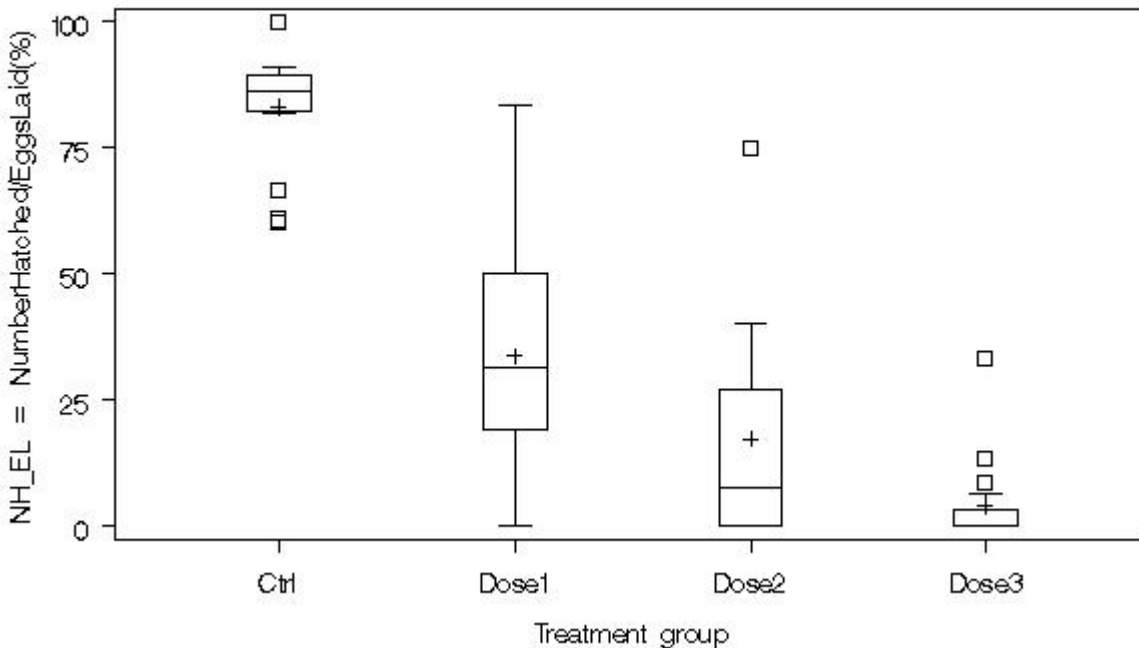
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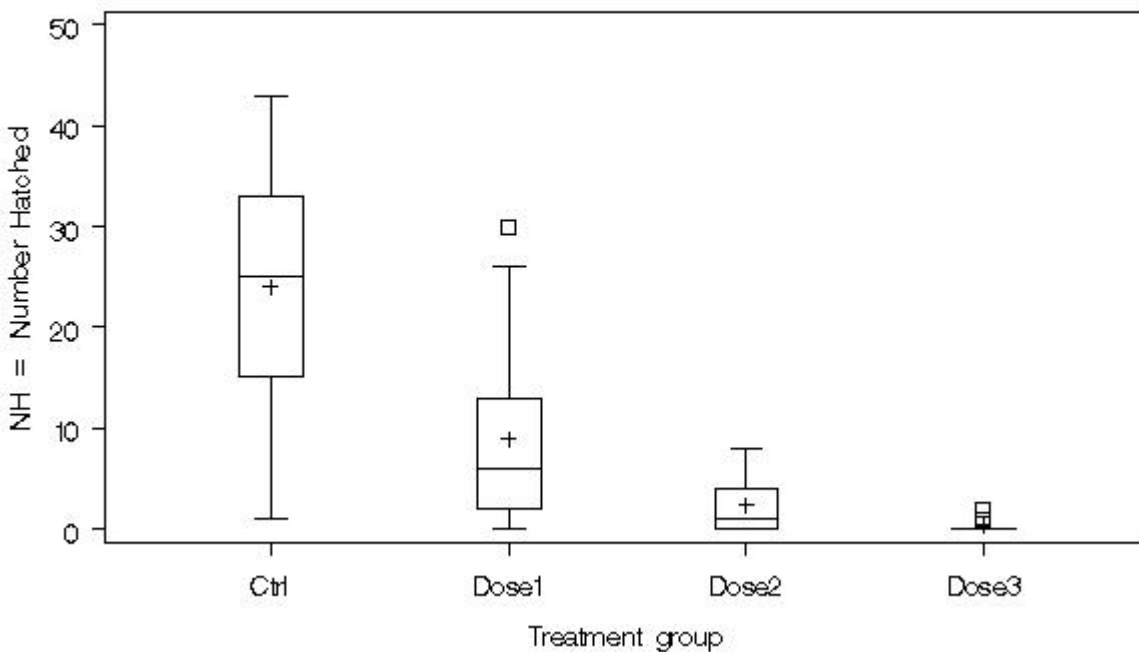
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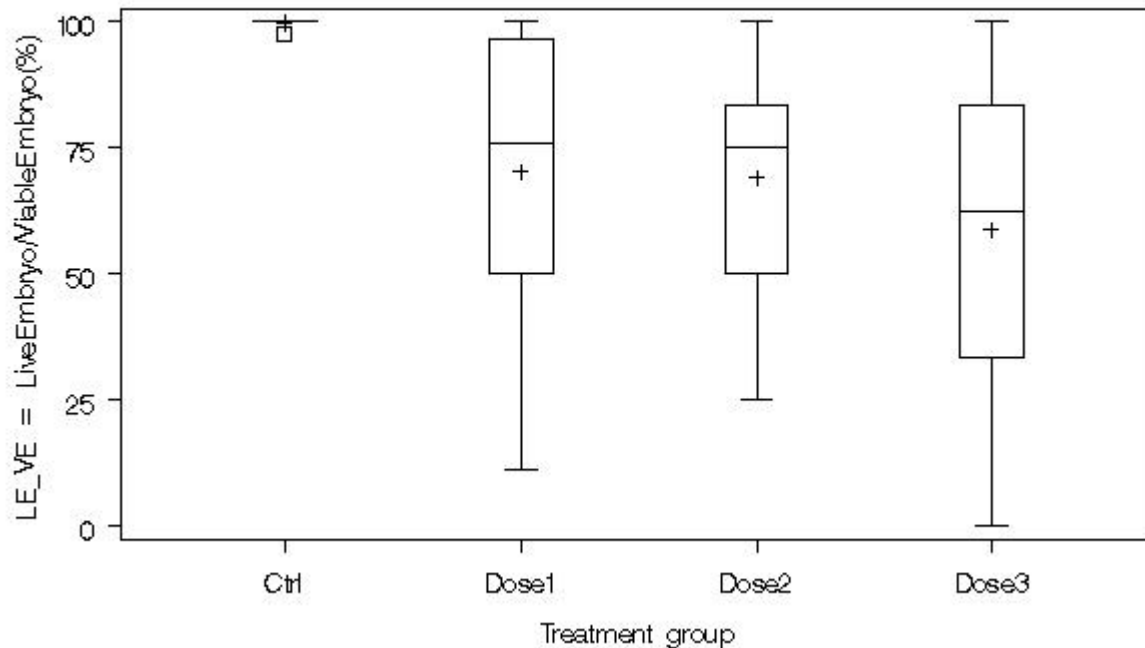
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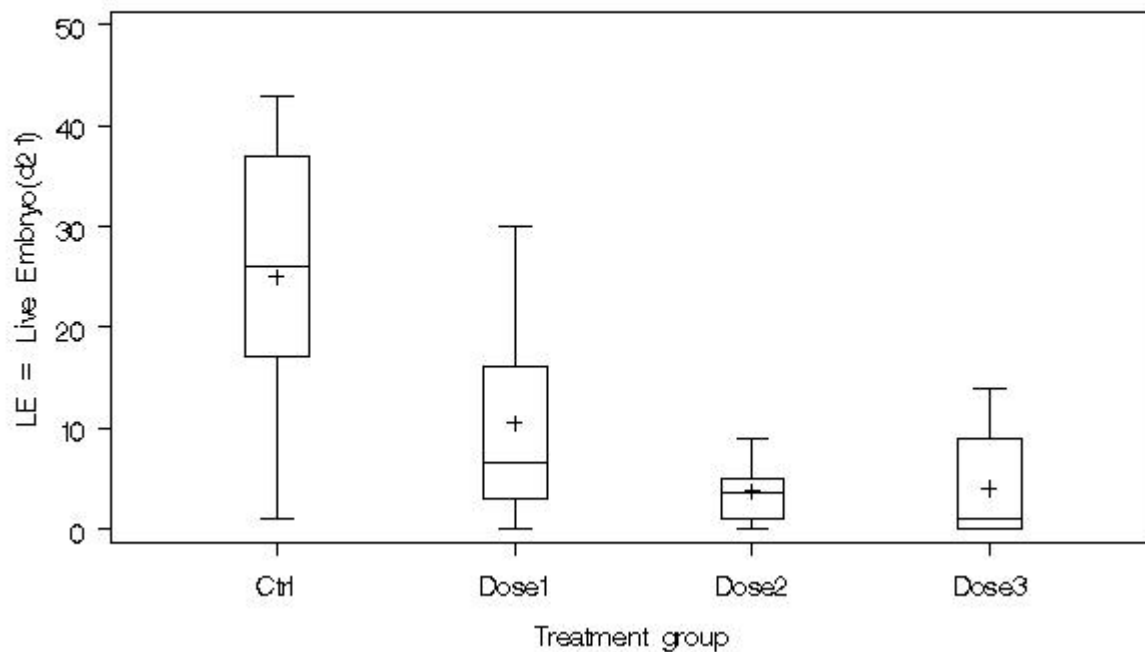
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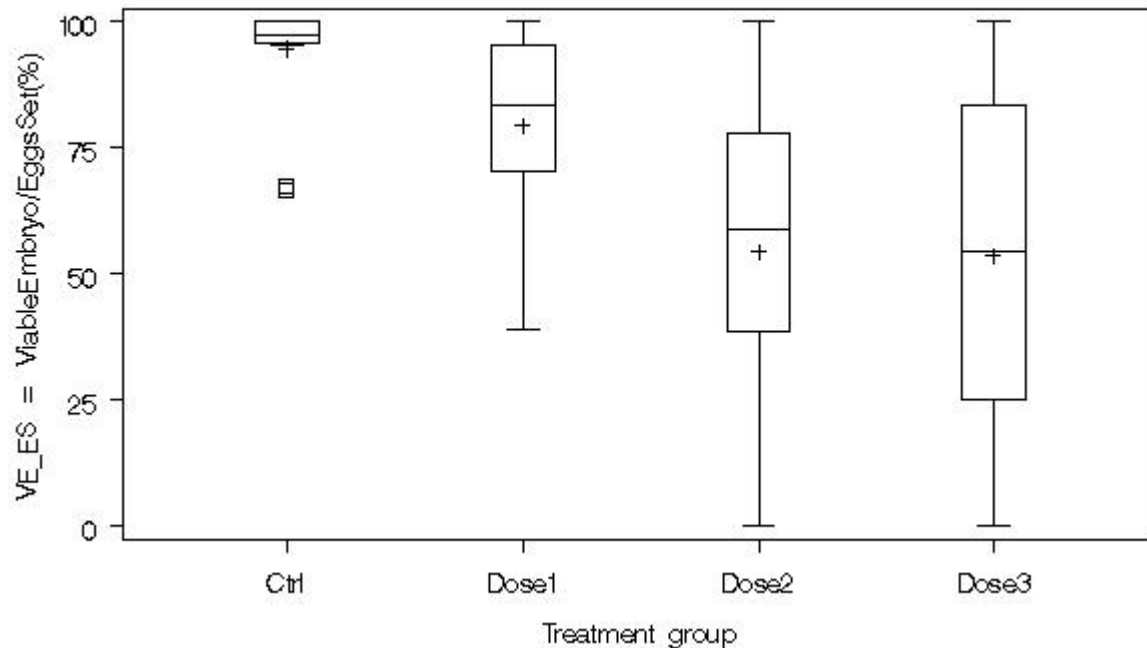
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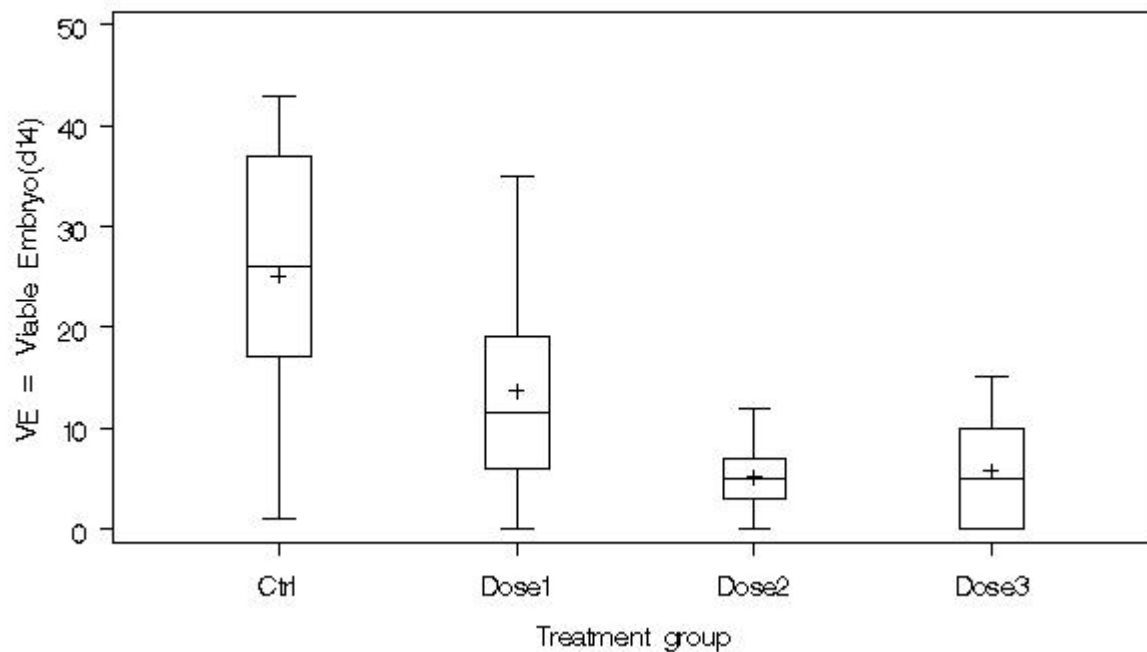
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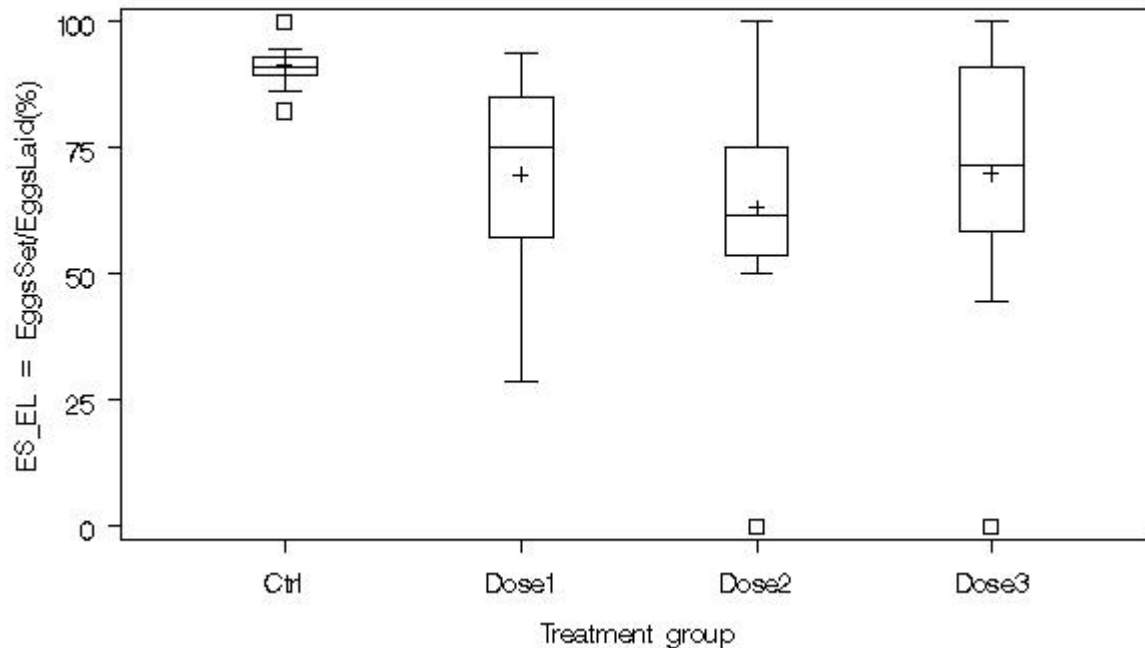
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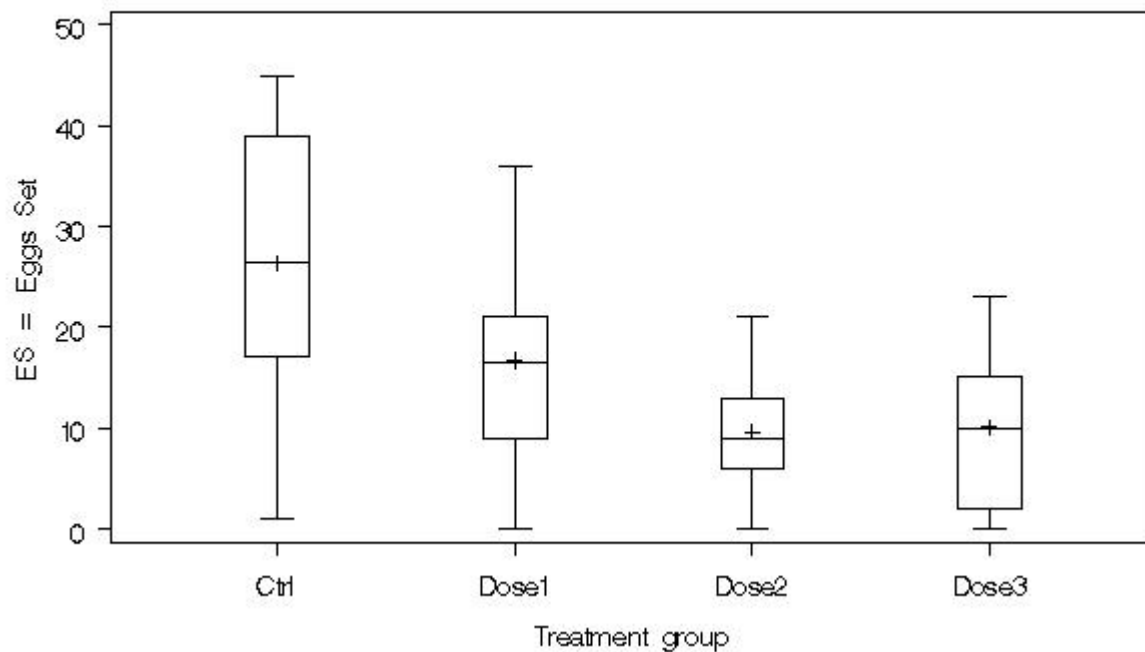
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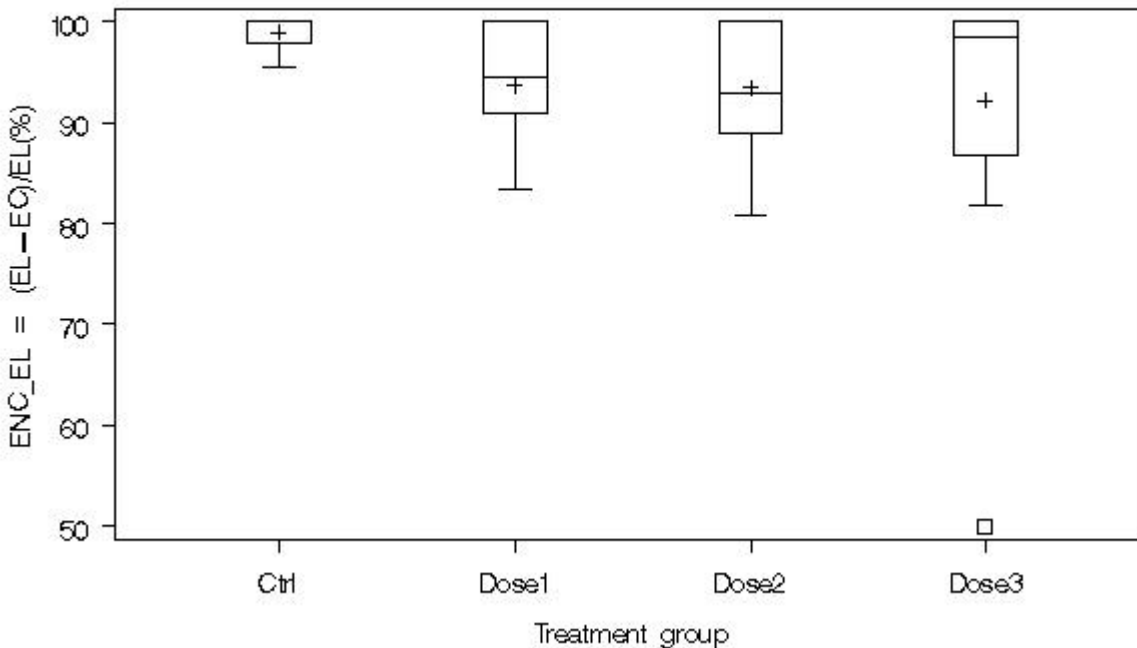
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Bobwhite repro, Fluopyram, MRID 47372345

